

Overview of COVID-19

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Epidemiology

The COVID-19 pandemic has exploded since cases were first reported in China in December 2019. As of February 22, 2022, more than 426 million cases of COVID-19—caused by SARS-CoV-2 infection—have been reported globally, including more than 5.8 million deaths.¹

Individuals of all ages are at risk for SARS-CoV-2 infection and severe disease. However, the probability of serious COVID-19 disease is higher in people aged ≥ 60 years, those living in a nursing home or long-term care facility, and those with chronic medical conditions. In an analysis of more than 1.3 million laboratory-confirmed cases of COVID-19 that were reported in the United States between January and May 2020, 14% of patients required hospitalization, 2% were admitted to the intensive care unit, and 5% died.² The percentage of patients who died was 12 times higher among those with reported medical conditions (19.5%) than among those without medical conditions (1.6%), and the percentage of those who were hospitalized was 6 times higher among those with reported medical conditions (45.4%) than among those without medical conditions (7.6%). The mortality rate was highest in those aged >70 years, regardless of the presence of chronic medical conditions. Among those with available data on health conditions, 32% had cardiovascular disease, 30% had diabetes, and 18% had chronic lung disease. Other conditions that may lead to a high risk for severe COVID-19 include cancer, kidney disease, liver disease (especially in patients with cirrhosis), obesity, sickle cell disease, and other immunocompromising conditions. Transplant recipients and pregnant people are also at a higher risk of severe COVID-19.³⁻¹⁰

Data from the United States suggest that racial and ethnic minorities experience higher rates of COVID-19 and subsequent hospitalization and death.¹¹⁻¹⁵ However, surveillance data that include race and ethnicity are not available for most reported cases of COVID-19 in the United States.^{4,16} Factors that contribute to the increased burden of COVID-19 in these populations may include over-representation in work environments that confer higher risks of exposure to COVID-19, economic inequality (which limits people's ability to protect themselves against COVID-19 exposure), neighborhood disadvantage,¹⁷ and a lack of access to health care.¹⁶ Structural inequalities in society contribute to health disparities for racial and ethnic minority groups, including higher rates of comorbid conditions (e.g., cardiac disease, diabetes, hypertension, obesity, pulmonary diseases), which further increases the risk of developing severe COVID-19.¹⁵

SARS-CoV-2 Variants

Like other RNA viruses, SARS-CoV-2 is constantly evolving through random mutations. New mutations can potentially increase or decrease infectiousness and virulence. In addition, mutations can increase the virus' ability to evade adaptive immune responses from past SARS-CoV-2 infection or vaccination. This may increase the risk of reinfection or decrease the efficacy of vaccines.¹⁸ There is evidence that some SARS-CoV-2 variants have reduced susceptibility to plasma from people who were previously infected or immunized, as well as to certain monoclonal antibodies (mAbs) that are being considered for prevention and treatment.¹⁹⁻²¹

Since December 2020, several variants have been identified that have now been assigned Greek letter designations by the World Health Organization (WHO). SARS-CoV-2 variants are designated as variants of concern (VOC) if they display certain characteristics, such as increased transmissibility or virulence. In addition, vaccines and/or therapeutics may have decreased effectiveness against VOC, and the mutations found in these variants may interfere with diagnostic test targets. The designation variant of interest (VOI) is used for important variants that have not yet been fully characterized; however, the

designations and definitions for these variants differ between organizations.^{22,23} In September 2021, the Centers for Disease Control and Prevention (CDC) added a new designation for variants: [variants being monitored](#) (VBM). This refers to variants for which the data indicate a potential or clear impact on approved or authorized medical countermeasures, or variants that have been associated with more severe disease or increased transmission rates; however, these variants are either no longer detected or are circulating at very low levels in the United States. As such, these variants do not pose a significant and imminent risk to public health in the United States.

The B.1.1.529 (Omicron) variant was designated a VOC in November 2021 and rapidly became the dominant variant across the globe. The Omicron VOC is more transmissible than other variants and is not susceptible to some of the anti-SARS-CoV-2 mAbs that have been developed for treatment and prevention.^{20,21,24} The Omicron VOC replaced the B.1.617.2 (Delta) variant, which was first identified in India and became the dominant variant in the United States after the summer of 2021.²⁵

Earlier variants included the B.1.1.7 (Alpha) variant, which was first seen in the United Kingdom and has been shown to be highly infectious and possibly more virulent than previously reported variants.²⁶⁻²⁸ The B.1.351 (Beta) variant was originally identified in South Africa, and the P.1 (Gamma) variant was identified in Manaus, Brazil. Both of these demonstrated reduced susceptibility to select anti-SARS-CoV-2 mAbs used for treatment and prevention. While the Alpha, Beta, and Gamma variants were previously designated as VOC, they have largely disappeared worldwide. For a detailed discussion on the susceptibility of certain VOC, VOI, and VBM to available anti-SARS-CoV-2 mAbs, please see [Anti-SARS-CoV-2 Monoclonal Antibodies](#).

The data on the emergence, transmission, and clinical relevance of these new variants is rapidly evolving; this is especially true for research on how variants might affect transmission rates, disease progression, vaccine development, and the efficacy of current therapeutics. Because the research on variants is moving quickly and the classification of the different variants may change over time, websites such as the CDC [COVID Data Tracker](#), [CoVariants.org](#), and [WHO's Tracking SARS-CoV-2 Variants](#) provide regular updates on the data for SARS-CoV-2 variants. The COVID-19 Treatment Guidelines Panel reviews the emerging data on these variants, paying particular attention to research on the impacts of these variants on testing, prevention, and treatment.

Clinical Presentation

The estimated incubation period for COVID-19 is up to 14 days from the time of exposure, with a median incubation period of 4 to 5 days.^{6,29,30} The spectrum of illness can range from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome and death. Among 72,314 people with COVID-19 in China, 81% of cases were reported to be mild (defined in this study as no pneumonia or mild pneumonia), 14% were severe (defined as dyspnea, respiratory frequency ≥ 30 breaths/min, oxygen saturation [SpO_2] $\leq 93\%$, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen [$\text{PaO}_2/\text{FiO}_2$] < 300 mm Hg, and/or lung infiltrates $> 50\%$ within 24 to 48 hours), and 5% were critical (defined as respiratory failure, septic shock, and/or multiorgan dysfunction or failure).³¹ In a report on more than 370,000 confirmed COVID-19 cases with reported symptoms in the United States, 70% of patients experienced fever, cough, or shortness of breath, 36% had muscle aches, and 34% reported headaches.² Other reported symptoms have included, but are not limited to, diarrhea, dizziness, rhinorrhea, anosmia, dysgeusia, sore throat, abdominal pain, anorexia, and vomiting.

The abnormalities seen in chest X-rays of patients with COVID-19 vary, but bilateral multifocal opacities are the most common. The abnormalities seen in computed tomography of the chest also vary, but the most common are bilateral peripheral ground-glass opacities, with areas of consolidation developing later in the clinical course of COVID-19.³² Imaging may be normal early in infection and can

be abnormal in the absence of symptoms.³²

Common laboratory findings in patients with COVID-19 include leukopenia and lymphopenia. Other laboratory abnormalities have included elevated levels of aminotransferase, C-reactive protein, D-dimer, ferritin, and lactate dehydrogenase.

Although COVID-19 is primarily a pulmonary disease, emerging data suggest that it also leads to cardiac,^{33,34} dermatologic,³⁵ hematologic,³⁶ hepatic,³⁷ neurologic,^{38,39} renal,^{40,41} and other complications. Thromboembolic events also occur in patients with COVID-19, with the highest risk occurring in critically ill patients.⁴²

The long-term sequelae of COVID-19 survivors are currently unknown. Persistent symptoms after recovery from acute COVID-19 have been described (see [Clinical Spectrum of SARS-CoV-2 Infection](#)). Lastly, SARS-CoV-2 infection has been associated with a potentially severe inflammatory syndrome in children (multisystem inflammatory syndrome in children, or MIS-C).^{43,44} Please see [Special Considerations in Children](#) for more information.

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